PATENT USSN: 10/560,296

Atty Dkt: 034176.004

REMARKS

The Official action mailed 30 September 2008, has been received and its contents carefully noted. The pending claims, claims 2-11, were rejected. Reconsideration in view of the following remarks is respectfully requested.

Priority Claim

Applicants respectfully submit that since the priority dates of the instant application are not relied upon for overcoming the art of record, no English translations are necessary. Should the Examiner disagree, Applicants respectfully request that the Examiner so indicate.

Rejection under 35 U.S.C. 103(a)

The Examiner rejected claims 2-12 under 35 U.S.C. 103(a) as being unpatentable over Li (CN J. Biochem. Pharma, 2002, 23(3):132-133) in view of Yokota (JP 63-182304) and Kolupavev (Fizilogia, 1991, 23(3):267-274). Specifically, the Examiner deemed that it would have been obvious to use microwave radiation to make chitosan oligomers according to the claimed invention.

Applicants respectfully submit that the reaction according to the present invention is a homogeneous reaction which is not taught or suggested by the three cited documents, Li, Yokota, or Kolupavev, alone or in combination. In particular, the cited documents do not teach or suggest using dilute hydrochloric acid to dissolve chitosan and using another electrolyte to increase the speed of degradation. In addition, the cited documents do not teach or suggest that the molecular weight of degraded chitosan obtained by microwave irradiation assisted with electrolytes is lower as compared with that obtained by microwave irradiation without electrolytes.

Applicants respectfully point out that the reaction of Li is a heterogeneous reaction, that is chitosan is dip in peroxide solution for several minutes, then it is subjected to a microwave irradiation. The peroxide solution of Li is not the same as the electrolyte solution according to the claimed invention. In addition, Li suggests that a carboxymethyl crosslinking reaction may be used in place of microwave irradiation. Thus, Li does not teach or suggest the requirement for

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microwave irradiation.

Yokata also relates to a heterogenous reaction as Yokata discloses the hydrolysis of chitosan in the presence of a system consisting of organic solvent (alcohol), water and mineral acid (dense hydrochloric acid). It should be noted, that the mineral acid was used to only slightly degrade chitosan in traditional reaction conditions (which are not the conditions set forth in the instant claims).

Kolupeav discloses that <u>sublethal</u> NaCl concentration applied to winter wheat coleopeiles induce an increase in invertase activity and intense hydrolysis of oligosaccharides. <u>Sublethal</u> NaCl apparently induces physiological changes associated with adaptation. In this case, it makes the hydrolysis of oligosaccharides not polysaccharides, such as chitosan. However, it should be noted that <u>lethal</u> NaCl concentrations <u>inhibited the enzyme and prevented hydrolysis of oligosaccharides</u>. Since Kolupeav mentions nothing about chitosan and the opposite effects lethal and sublethal NaCl concentrations have on oligosaccharides, one of ordinary skill in the art would not expect that NaCl will degrade chitosan with a reasonable likelihood of success. In addition Kolupeav mentions nothing about the purpose/activity of NaCl such that one of ordinary skill in the art would be motivated to use KCl or CaCl₂ in order to increase the degradation speed of chitosan according to the present invention.

Since the cited documents do not teach or suggest a homogenous reaction wherein chitosan dissolved in an electrolyte solution comprising an acid and an electrolyte (to speed up the rate of degradation) is subjected to microwave irradiation, the claimed invention is novel and unobvious. Nowhere do the cited references teach or suggest the necessity of the electrolyte assisted degradation. In particular, the cited documents do not teach or suggest that the molecular weight of degraded chitosan made according to the present invention is lower as compared with that obtained by microwave irradiation without electrolytes.

Tables 1-8 of the present specification show that chitosan oligomers having a molecular weight ranging from 600-30000 Da was obtained according to the instant inventive method. Applicants respectfully submit that a person having ordinary skill in the art would not have expected that chitosan oligomers having molecular weights ranging from 600-30000 Da could be obtained by combining the disclosures of Li, Yokata and Kolupeav, with a reasonable

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expectation of success for the following reasons:

1. Extensive (non-routine) experimentation was required to select the particular dissolving acid, electrolyte, the concentration of electrolyte, time and microwave power that gives the desired molecular weight, i.e. 600-30000 Da. As shown in tables 1-8, different electrolytes have different effects on the degradation of chitosan. See for example, the influence of CaCl₂ as compared to that of NaCl.

- 2. Nowhere do the cited documents teach or suggest that the method of the instant invention will be more economical over conventional methods and will result in chitosan of a desired molecular weight which makes the chitosan water soluble. See specification, page 2.
- 3. The cited documents provide no suggestion that chitosan can be successfully degraded by (1) a dilute acid and (2) the speed of degradation can be increased by microwave irradiation and (3) an electrolyte. Chitosan being degraded by dense hydrochloric acid within several hours is a well-known fact. However, there is no evidence that chitosan can be effectively degraded by a dilute acid. When chitosan is dissolved in dilute acid, the degradation speed of chitosan is very slow by traditional heating reaction, even after 24 hours the change of molecular weight is only slight. Nowhere do the cited documents teach or suggest that the amount and rate of degradation can be increased by microwave irradiation. Thus, one of ordinary skill in the art would not have expected that the degradation speed of chitosan dissolved in dilute acid would be increased by microwave irradiation reaction with a reasonable likelihood of success. In addition, because Kolupeav mentions nothing about chitosan and the opposite effects lethal and sublethal NaCl concentrations have on oligosaccharides, one of ordinary skill in the art would not expect that NaCl or any other electrolyte such as KCl or CaCl₂ will degrade chitosan with a reasonable likelihood of success.

Therefore, Applicants respectfully submit that one of ordinary skill in the art would not have been motivated to combined the disclosures of the three documents with a reasonable likelihood of success in obtaining chitosan oligosaccharides having a molecular weight of 600-30000 Da according to the instant method as claimed. Thus, the present invention is novel and unobvious and the rejection under 35 U.S.C. 103(a) should properly be withdrawn.

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Request for Interview

Either a telephonic or an in-person interview is respectfully requested should there be any

remaining issues.

CONCLUSION

All of the stated grounds of objection and rejection have been properly traversed,

accommodated, or rendered moot. Therefore, it is respectfully requested that the Examiner

reconsider all presently outstanding objections and rejections and that they be withdrawn. It is

believed that a full and complete response has been made to the outstanding Official action and,

as such, the present application is in condition for allowance. If the Examiner believes, for any

reason, that personal communication will expedite prosecution of this application, the Examiner

is invited to telephone the undersigned at the number provided.

It is not believed that extensions of time are required, beyond those that may otherwise be

provided for in accompanying documents. However, in the event that additional extensions of

time are necessary to prevent abandonment of this application, then such extensions of time are

hereby petitioned under 37 C.F.R. 1.136(a), and any fees required therefor are hereby authorized

to be charged to **Deposit Account No. 02-4300**, Attorney Docket No. **034176.004**.

Respectfully submitted,

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